

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nika Adham, et al.  
Serial No.: 09/116,676 Examiner: G. Draper  
Filed: July 16, 1998 Group Art Unit: 1647  
For: DNA ENCODING A HUMAN OB RECEPTOR (OB-RE) AND  
USES THEREOF

1185 Avenue of the Americas  
New York, New York 10036

Assistant Commissioner for Patents  
Washington, D.C. 20231

SIR:

**DECLARATION OF NIKA ADHAM, BETH BOROWSKY,  
NIGEL LEVENS, AND RADEK C. SKODA  
UNDER 37 C.F.R. §1.131.**

We, Nika Adham, Beth Borowsky, Nigel Levens, and Radek C. Skoda,  
hereby declare as follows:

1. We conceived of the invention claimed in the above-identified patent application, i.e., a process for determining whether a chemical compound specifically binds to a soluble polypeptide with specific properties as recited in claim 224 as amended in the Amendment filed concurrently with the filing of the Declaration (the "Binding Assay").
2. Prior to December 31, 1996, a Binding Assay was performed by Noel Boyle under the direction and supervision of coinventor Nika Adham in the United States at the laboratories of Synaptic Pharmaceutical Corporation, an assignee of record of the subject application. Copies of pages 189 and 190 of Noel Boyle's notebook number 11914 and pages 2-7 of Noel Boyle's notebook number 11915 detailing the performance of such a Binding Assay for determining whether leptin specifically binds to human Ob-Re, a soluble polypeptide as recited in claim 224 are attached hereto as **Exhibit A**. Although the dates have been redacted from these

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notebook pages, all dates ar prior to December 31, 1996. Thus, at least one embodiment of the invention claimed was reduced to practice in the United States prior to December 31, 1996.

3. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1/29/01  
Date

Nika Adham  
Nika Adham

\_\_\_\_\_  
Date

\_\_\_\_\_  
Beth Borowsky

\_\_\_\_\_  
Date

\_\_\_\_\_  
Nigel Levens

\_\_\_\_\_  
Date

\_\_\_\_\_  
Radek C. Skoda

(<sup>125</sup>I) Leptin = 0.1 nM (F)

100,000 cpm/μl

Dry plate

Non-specific  $1 \times 10^{-6}$  M (B) cold leptin

MAKE 8 ml (<sup>125</sup>I)Leptin

58.9 μCi / 0.1 ml 1840 Ci/mole

$$\frac{58.9 \mu\text{Ci/ml} \times 287}{1.840 \times 10^9 \mu\text{Ci/mole}} = \frac{169}{1.840 \times 10^9} = 9.19 \times 10^{-8} \frac{\text{mole}}{\text{ml}}$$

$$9.19 \times 10^{-8} \frac{\text{mole}}{\text{ml}} \cdot V = 1 \times 10^{-9} \frac{\text{mole}}{\text{ml}} \cdot 8 \text{ ml}$$

$$V = 8.2 \text{ ml}$$

Read & Understood by me,

Date

Invented by

Date

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Recorded by

TITLE Leptin Via Scintillation Proximity Assay Project

189

From Page No. \_\_\_\_\_

Protocol #: 13

Count time (minutes): 1.00  
Assay Type: CPM  
Background Subtract: IPA 84g  
Outlier: 5.0 FLAG  
Screening: OFF

Window A  
Nuclide: I-125  
Half Life (hours): 0.00  
Multiplier: 1.0000  
ICV Flag Limit: 0.00

WARNING: NOT BACKGROUND DATA

S# A:CPM A:ZERR B:CPM B:ZERR  
1 123406 0.28 0.0  
3 MISSING TUBE(S)

Table 1. Assay protocol

	Non-specific binding (NSB)	Zero standard (B <sub>0</sub> )	Standards	Test	Solvent Control
Buffer	-	50µl	-	-	-
Standards	50µl	-	50µl	-	-
Test Compound	-	-	-	50µl	-
Tracer	50µl	50µl	50µl	50µl	50µl
Test Solvent*	-	-	-	-	50µl
Cell preparation	50µl	50µl	50µl	50µl	50µl
WGA SPA beads	50µl	50µl	50µl	50µl	50µl
Cap tubes, shake overnight (16-24hr) at room temperature (15-30°C) Leave to settle for 1 hour					
Count in scintillation counter					

\* For example in organic solvents add the relevant solvent

To Page No. \_\_\_\_\_

Witnessed &amp; Understood by me,

Date

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Date

TITLE SPA LEPTIN SOURCE MEMBRANES Project No.             
B ok No.           

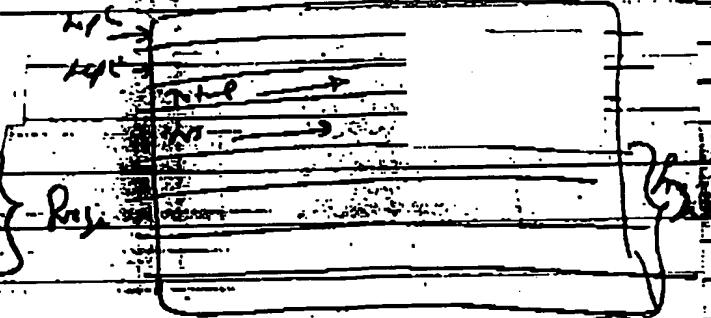
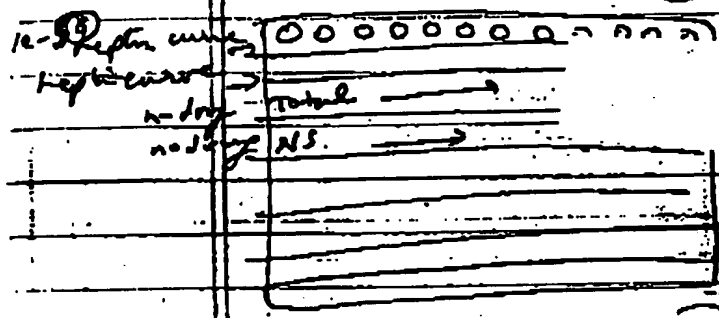
From Page No.           

SPA binding on Oble -

Assay buffer: use leptin binding assay buffer + 1% BSA

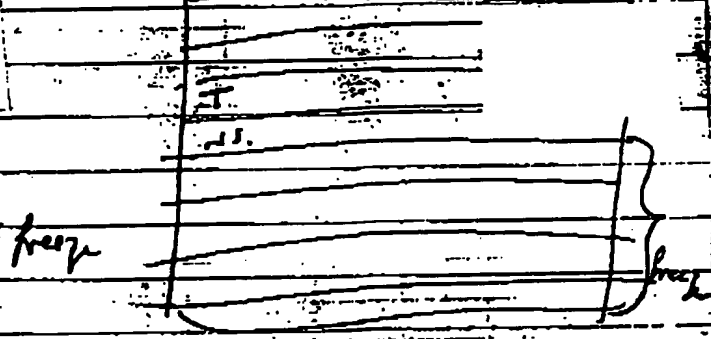
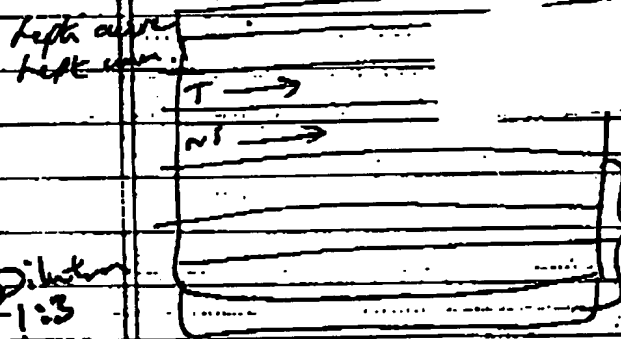
Oble (medium) ①

Mock (mock) ②

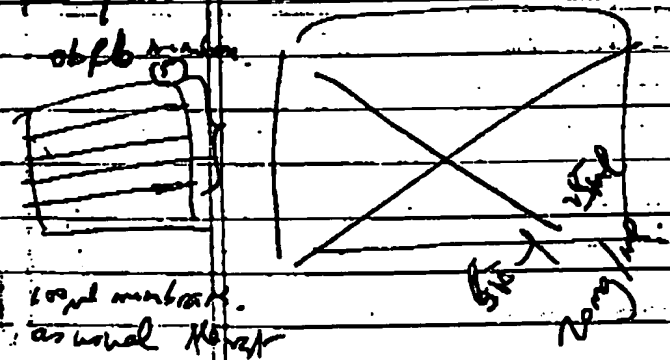


Oble (optimum) ③

Oble (medium) ④



Dilution 1:3



round  
2nd hand  
2nd Dryer total

Add 5th bead

room temp other overnight

Witnessed & Understood by me,            Date            Initialed by            Date             
Recorded by           

To Page No.

Project No. \_\_\_\_\_

Book No. \_\_\_\_\_

TITLE SPA LGPT in Soluble Membranes.

From Page No. \_\_\_\_\_

SPA

Plate 1 - hob.Re ++

Plate 2 - hob.Re # mock

Plate 3 - [cos 7] hob.Re, # B025 P91 (optimum medium) 1:2

Plate 4 - [cos 7] hob.Re, # B025 P91 (normal medium) 1:2

Plate 5 - [Cos 7] hob.Re, # B07 P55

Lol = 2.4 (1:3)

Witnessed &amp; Understood by me,

Date

ventated by

Date

Recorded by

To Page No. \_\_\_\_\_

**Project No.**

**Revised No**

5

TITLE	POS	TIME	IC#	1251	LUMEX	ELAPSED	
NO		MIN		CPM	%	TIME	
101	**1	1.00	6.461	2297.06	4.18	0.00	222.19
102	**2	1.00	6.173	1735.09	4.81	0.01	223.54
103	**3	1.00	6.497	1296.32	5.56	0.01	224.89
104	**4	1.00	6.572	990.79	6.56	0.01	225.27
105	**5	1.00	6.511	859.56	6.83	0.01	227.62
106	**6	1.00	6.541	825.51	6.97	0.01	228.97
107	**7	1.00	6.510	2527.64	3.98	0.01	230.34
108	**8	1.00	6.547	2490.60	4.01	0.00	231.69
109	**9	1.00	6.477	2621.87	3.91	0.00	233.04
110	**10	1.00	6.502	2564.79	3.95	0.01	234.42
111	**11	1.00	6.368	2810.28	3.78	0.00	235.77
112	**12	1.00	6.265	2798.28	3.78	0.01	237.12
113	**13	1.00	6.484	2657.05	3.86	0.00	238.49
114	**14	1.00	6.390	2885.51	3.73	0.00	239.84
115	**15	1.00	6.518	2926.62	3.70	0.01	241.19
116	**16	1.00	6.521	2830.47	3.76	0.01	242.57
117	**17	1.00	6.437	2753.35	3.82	0.01	243.92
118	**18	1.00	6.506	2573.03	3.95	0.01	245.27
119	**1	1.00	6.389	728.43	7.42	0.01	246.74
120	**2	1.00	7.048	714.41	7.49	0.02	248.09
121	**3	1.00	6.528	740.47	7.36	0.02	249.44
122	**4	1.00	6.786	789.58	7.12	0.01	250.82
123	**5	1.00	7.000	765.54	7.24	0.02	252.17
124	**6	1.00	6.549	774.56	7.19	0.01	253.52
125	**7	1.00	6.837	705.43	7.54	0.02	254.89
126	**8	1.00	6.982	780.99	7.17	0.02	256.24
127	**9	1.00	6.584	705.45	7.54	0.02	257.59
128	**10	1.00	6.770	756.56	7.28	0.01	258.95
129	**11	1.00	6.566	777.61	7.18	0.03	260.32
130	**12	1.00	6.929	759.58	7.26	0.02	261.65
131	**13	1.00	7.145	10135.24	1.99	0.00	263.04
132	**14	1.00	7.162	2546.36	3.97	0.01	264.39
133	**15	1.00	7.004	9852.86	2.02	0.00	265.74
134	**16	1.00	6.560	9620.47	2.04	0.00	267.11
135	**17	1.00	7.184	9693.73	2.03	0.00	268.46
136	**18	1.00	7.138	9917.31	2.01	0.00	269.81
137	**1	1.00	7.065	9112.69	2.10	0.00	271.29
138	**2	1.00	7.036	6454.02	2.49	0.00	272.64
139	**3	1.00	7.113	4094.94	3.13	0.01	273.99
140	**4	1.00	6.945	3018.62	3.64	0.00	275.36
141	**5	1.00	7.512	2743.05	3.82	0.00	276.71
142	**6	1.00	6.900	2571.70	3.95	0.00	278.05
143	**7	1.00	6.937	9689.67	2.03	0.00	279.44
144	**8	1.00	7.075	2111.72	4.36	0.01	280.79
145	**9	1.00	7.205	9980.43	2.00	0.00	282.14
146	**10	1.00	7.198	10414.52	1.96	0.00	283.51
147	**11	1.00	6.945	9862.38	2.02	0.00	284.86
148	**12	1.00	6.996	9835.42	2.02	0.00	286.21
149	**13	1.00	7.020	9442.63	2.06	0.00	287.59
150	**14	1.00	7.087	6677.37	2.48	0.00	288.94</

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Date \_\_\_\_\_

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Project No.

Loplin Soluble machines

PAGE: 1

SAM NO	POS	TIME MIN	IC#	1251		LUMEX %	ELAPSED TIME
				CPM	%ERROR		
105	**15	1.00	6.749	1720.96	4.82	0.01	142.99
106	**16	1.00	6.994	1274.46	5.61	0.02	144.36
107	**17	1.00	7.078	1013.17	6.29	0.01	145.70
108	**18	1.00	6.841	989.16	6.36	0.01	147.05
109	**1	1.00	6.536	3233.82	3.52	0.00	148.54
110	**2	1.00	6.808	862.03	6.82	0.02	149.89
111	**3	1.00	6.791	4667.62	2.93	0.00	151.24
112	**4	1.00	6.839	3698.49	3.29	0.00	152.61
113	**5	1.00	6.664	4233.19	3.08	0.00	153.96
114	**6	1.00	6.871	3384.18	3.44	0.00	155.31
115	**7	1.00	6.896	3795.73	3.25	0.00	156.69
116	**8	1.00	7.171	2439.07	4.05	0.00	158.04
117	**9	1.00	7.104	1767.24	4.76	0.01	159.39
118	**10	1.00	6.970	1076.38	6.10	0.01	160.76
119	**11	1.00	7.187	864.11	6.81	0.01	162.10
120	**12	1.00	6.686	984.28	6.38	0.02	163.46
121	**13	1.00	6.759	5354.02	2.74	0.00	164.84
122	**14	1.00	6.855	4320.72	3.04	0.00	166.19
123	**15	1.00	6.895	3913.22	3.20	0.00	167.54
124	**16	1.00	6.852	4462.00	3.00	0.00	168.91
125	**17	1.00	6.848	4448.03	3.00	0.00	170.26
126	**18	1.00	6.895	4898.69	2.86	0.00	171.61
127	**1	1.00	6.836	5364.39	2.73	0.00	173.09
128	**2	1.00	7.120	5314.38	2.75	0.00	174.44
129	**3	1.00	6.866	4718.60	2.91	0.00	175.79
130	**4	1.00	6.750	4763.72	2.90	0.00	177.16
131	**5	1.00	6.787	4473.36	2.99	0.00	178.51
132	**6	1.00	6.598	5404.74	2.72	0.00	179.86
133	**7	1.00	7.420	963.39	6.45	0.01	181.24
134	**8	1.00	7.475	847.23	6.86	0.02	182.59
135	**9	1.00	7.183	865.27	6.80	0.02	183.94
136	**10	1.00	7.585	809.19	7.04	0.02	185.30
137	**11	1.00	7.372	835.24	6.93	0.02	186.65
138	**12	1.00	7.245	905.36	6.65	0.02	188.01
139	**13	1.00	7.717	829.25	6.95	0.01	189.39
140	**14	1.00	7.334	823.25	6.98	0.01	190.74
141	**15	1.00	7.186	878.34	6.75	0.01	192.09
142	**16	1.00	7.266	807.24	7.04	0.01	193.45
143	**17	1.00	7.436	993.54	6.35	0.01	194.80
144	**18	1.00	6.908	1018.59	6.27	0.01	196.15
145	**1	1.00	6.312	2363.72	4.12	0.00	197.64
146	**2	1.00	6.683	803.27	7.06	0.01	198.99
147	**3	1.00	6.538	2331.72	4.15	0.01	200.34
148	**4	1.00	6.341	2644.25	3.89	0.00	201.70
149	**5	1.00	6.488	2583.18	3.94	0.00	203.06
150	**6	1.00	6.486	2725.44	3.83	0.01	204.41
151	**7	1.00	6.632	2159.54	4.31	0.01	205.79
152	**8	1.00	6.725	1890.12	4.60	0.01	207.14
153	**9	1.00	6.934	1441.39	5.27	0.01	208.49
154	**10	1.00	6.915	949.39	6.50	0.01	209.85
155	**11	1.00	6.699	804.35	7.06	0.02	211.20
156	**12	1.00	6.557	774.31	7.16	0.01	212.55
157	**13	1.00	6.619	2376.05	4.11	0.01	213.94
158	**14	1.00	6.603	796.37	7.09	0.01	215.29
159	**15	1.00	6.418	2617.52	3.91	0.00	216.64
160	**16	1.00	6.540	2429.22	4.06	0.00	218.00
161	**17	1.00	6.346	2521.41	3.99	0.00	219.36
162	**18	1.00	6.273	2504.40	4.00	0.01	220.71

Witness:

led by

Opine ok

T=4780

N=881

Regule ned  
Okle

Lpt

Regule ned

Opine

Lpt



## Lepin soluble membranes

TITLE	SAM	POS	TIME	IC#	1 2 5 I	LUMEX	ECLIPSED
From P.	NO		MIN		CPM	%	TIME
	47	**11	1.00	5.951	790.40	7.12	63.90
	48	**12	1.00	5.511	694.36	7.58	65.25
	49	**13	1.00	5.759	456.24	7.57	66.64
	50	**14	1.00	5.752	848.46	6.87	67.97
	51	**15	1.00	5.932	523.29	8.75	69.34
	52	**16	1.00	5.143	551.31	8.52	70.70
	53	**17	1.00	5.821	517.30	8.80	72.05
	54	**18	1.00	5.782	542.32	8.59	73.40
	55	**1	1.00	6.896	577.34	8.33	74.89
	56	**2	1.00	6.307	428.26	9.67	76.24
	57	**3	1.00	5.909	533.33	8.66	77.59
	58	**4	1.00	5.996	493.31	9.01	78.95
	59	**5	1.00	6.075	521.33	8.76	80.30
	60	**6	1.00	5.425	345.22	10.77	81.65
	61	**7	1.00	5.346	684.45	7.65	83.04
	62	**8	1.00	6.001	757.51	7.27	84.39
	63	**9	1.00	5.880	755.51	7.28	85.72
	64	**10	1.00	5.927	788.55	7.12	87.10
	65	**11	1.00	5.825	901.63	6.66	88.45
	66	**12	1.00	5.973	797.57	7.08	89.81
	67	**13	1.00	6.264	807.58	7.04	91.19
	68	**14	1.00	6.368	765.86	7.23	92.54
	69	**15	1.00	6.138	801.60	7.07	93.89
	70	**16	1.00	6.385	766.58	7.23	95.25
	71	**17	1.00	6.255	787.60	7.13	96.60
	72	**18	1.00	5.925	830.65	6.94	97.95
	73	**1	1.00	6.061	732.58	7.39	99.42
	74	**2	1.00	5.934	738.89	7.36	100.77
	75	**3	1.00	5.994	703.57	7.54	102.12
	76	**4	1.00	5.710	657.54	7.80	103.50
	77	**5	1.00	6.291	503.42	8.92	104.85
	78	**6	1.00	6.647	456.39	9.37	106.20
	79	**7	1.00	6.552	466.40	9.26	107.57
	80	**8	1.00	6.639	494.43	9.00	108.92
	81	**9	1.00	6.056	860.75	6.82	110.27
	82	**10	1.00	5.902	726.65	7.42	111.65
	83	**11	1.00	6.462	808.73	7.04	113.00
	84	**12	1.00	6.495	644.52	7.88	114.35
	85	**13	1.00	6.222	771.71	7.20	115.72
	86	**14	1.00	6.174	739.69	7.36	117.07
	87	**15	1.00	6.219	644.61	7.88	118.42
	88	**16	1.00	6.132	540.52	8.61	119.80
	89	**17	1.00	6.709	394.38	10.08	121.15
	90	**18	1.00	6.737	545.53	8.57	122.50
	91	**1	1.00	6.458	624.62	8.01	123.97
	92	**2	1.00	6.216	568.97	8.39	125.32
	93	**3	1.00	6.198	728.73	7.41	126.67
	94	**4	1.00	6.151	763.78	7.24	128.05
	95	**5	1.00	6.245	883.91	6.73	129.40
	96	**6	1.00	6.383	787.82	7.13	130.75
	97	**7	1.00	6.125	5482.76	2.70	132.12
	98	**8	1.00	6.848	916.97	6.61	133.47
	99	**9	1.00	6.422	5008.37	2.83	134.82
	100	**10	1.00	6.311	4978.39	2.84	136.21
	101	**11	1.00	6.532	4710.15	2.92	137.56
	102	**12	1.00	6.668	4465.94	2.99	138.91
	103	**13	1.00	6.867	3962.42	3.18	140.27
	104	**14	1.00	6.909	2948.32	3.69	141.62

Recorded by

Nal Pal

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Sept 12-4

Project No. \_\_\_\_\_

Book No. \_\_\_\_\_

TITLE

Leptin Soluble machines

D: 125. I

From Page USER: 3

COMMENT:

PRESET TIME : 1.00  
 DATA CALC : CPM H# : NO SAMPLE REPEATS: 1 PRINTER  
 COUNT BLANK : NO IC# : YES REPLICATES : 1 RS232  
 TWO PHASE : NO AGC : NO CYCLE REPEATS : 1  
 SCINTILLATOR: LIQUID LUMEX: NO LOW SAMPLE REJ: 0  
 LOW LEVEL : NO HALF LIFE CORRECTION DATE: none

ISOTOPE 1: 125I %ERROR: 2.00 FACTOR: 1.000000 SKG. SUB: --

SAM NO	POS	TIME MIN	IC#	125I		LUMEX %	ELAPSED TIME
				CPM	%ERROR		
1 **-1		1.00	4.785	2278.01	4.19	0.01	1.25
2 **-2		1.00	5.337	762.01	7.25	0.02	2.62
3 **-3		1.00	4.913	2074.06	4.39	0.01	3.97
4 **-4		1.00	4.881	1816.07	4.69	0.01	5.34
5 **-5		1.00	4.830	1701.08	4.85	0.01	6.67
6 **-6		1.00	4.737	2115.13	4.35	0.01	8.02
7 **-7		1.00	4.802	1761.13	4.77	0.01	9.39
8 **-8		1.00	5.166	1416.12	5.31	0.01	10.74
9 **-9		1.00	5.067	11375.13	5.39	0.01	12.09
10 **-10		1.00	5.319	823.09	6.97	0.02	13.45
11 **-11		1.00	5.427	749.09	7.31	0.03	14.81
12 **-12		1.00	5.166	661.08	7.78	0.03	16.15
13 **-13		1.00	4.810	2520.34	3.98	0.01	17.52
14 **-14		1.00	5.642	688.10	7.62	0.02	18.87
15 **-15		1.00	4.991	1902.30	4.59	0.01	20.22
16 **-16		1.00	4.869	1859.31	4.64	0.01	21.60
17 **-17		1.00	5.028	1882.34	4.61	0.01	22.96
18 **-18		1.00	4.901	1900.36	4.59	0.01	24.30
19 **-1		1.00	4.927	2042.41	4.43	0.01	25.77
20 **-2		1.00	5.037	1492.32	5.18	0.01	27.12
21 **-3		1.00	5.180	1179.26	5.82	0.01	28.47
22 **-4		1.00	5.407	930.22	6.56	0.02	29.85
23 **-5		1.00	5.645	777.19	7.17	0.03	31.20
24 **-6		1.00	5.477	833.21	6.93	0.01	32.55
25 **-7		1.00	4.896	2788.74	3.79	0.01	33.92
26 **-8		1.00	5.175	2653.74	3.88	0.01	35.27
27 **-9		1.00	4.842	2310.67	4.16	0.01	36.62
28 **-10		1.00	4.901	2386.72	4.09	0.01	38.01
29 **-11		1.00	4.972	2022.63	4.45	0.01	39.36
30 **-12		1.00	4.852	1964.63	4.51	0.01	40.71
31 **-13		1.00	5.096	2824.94	3.76	0.01	42.07
32 **-14		1.00	5.028	2105.72	4.36	0.01	43.42
33 **-15		1.00	5.034	1995.71	4.48	0.01	44.77
34 **-16		1.00	5.152	1807.66	4.70	0.01	46.16
35 **-17		1.00	5.238	1874.70	4.62	0.01	47.51
36 **-18		1.00	4.993	2026.78	4.44	0.01	48.85
37 **-1		1.00	5.635	787.31	7.13	0.02	50.32
38 **-2		1.00	5.818	789.32	7.12	0.01	51.67
39 **-3		1.00	5.614	682.29	7.66	0.02	53.02
40 **-4		1.00	5.581	806.35	7.04	0.02	54.40
41 **-5		1.00	5.520	660.29	7.78	0.02	55.75
42 **-6		1.00	5.739	718.32	7.46	0.02	57.10
43 **-7		1.00	5.784	724.34	7.43	0.01	58.47
44 **-8		1.00	5.552	725.34	7.43	0.02	59.82
45 **-9		1.00	5.613	725.35	7.43	0.02	61.17
46 **-10		1.00	5.828	587.29	8.25	0.02	62.55

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Witnessed

Recorded by

Kul Jha